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MORPHOMETRIC ASPECTS OF STUDYING THE FEATURES OF REMODELING OF ATRIAL STRUCTURES AT POSTRESECTION PORTAL HYPERTENSION

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Abstract

Introduction. Removal of the left and right lateral lobes of the liver in white rats leads to postresection portal hypertension, which is characterized by dilation and plethora of the hepatic portal vein, mesenteric veins, esophageal and gastric veins, veins of the anterior abdominal wall, splenomegaly, ascites and multiorgan failure.

Objective of the research: to study the features of remodeling of the structures of the atria at postresection portal hypertension histostereometrically.

Materials of the research and their discussion. The peculiarities of remodeling the structures of the atria were histostereometrically studied in 65 adult white male rats, which were divided into 3 groups: the 1- consisted of 20 intact animals, the 2 – 30 rats with postresection portal hypertension, which was modeled by removal of the left and right lateral lobes of the liver, the 3 – 15 animals with postresection portal hypertension and multiorgan failure. One month after the start of the experiment, rats were euthanized by bloodletting under conditions of thiopental anesthesia. Histological micropreparations were used to

determine the diameters of cardiomyocytes of the left and right atria, diameters of their nuclei, nuclear-cytoplasmic relations, relative volumes of cardiomyocytes, capillaries, stroma, stromal-cardiomyocyte, capillary-cardiomyocyte relations, relative volumes of damaged cardiomyocytes. Quantitative indicators were processed statistically.

Results of the research and their discussion. Histostereometrically, it was found that postresection portal hypertrophy leads to hypertrophy of atrial cardiomyocytes, their nuclei, growth of stromal structures, relative volumes of damaged cardiomyocytes, disorders of tissue and cellular structural homeostasis. The revealed features of remodeling of the studied structures dominated in the left atrium at combination of postresection portal hypertension with multiorgan failure.

Conclusions. Postresection portal hypertension leads to pronounced remodeling of the structures of the left and right atria, characterized by hypertrophy of cardiomyocytes, changes in their nuclear-cytoplasmic relations, an increase of the relative volume of stroma, damaged cardiomyocytes, pronounced disorders of tissue and cellular structural homeostasis. The revealed morphological changes dominated in the left atrium at combination of postresection portal hypertension with multiorgan failure.

Key words: postresection portal hypertension; histostereometry; atria.

Introduction. Today, liver resection is often performed in surgical clinics in benign and malignant tumors, metastases, liver injuries, intrahepatic cholangiolithiasis, alveolar echinococcosis, liver transplantation. Removal of large volumes of liver parenchyma can lead to postresection portal hypertension. The latter is complicated by bleeding from varicose veins of the esophagus and stomach, rectum, ascites, splenomegaly, secondary hypersplenism, parenchymal jaundice, portosystemic encephalopathy, multiorgan failure [3, 8, 10]. In portal hypertension, the organs from which venous outflow is carried out into the portal hepatic vein, which play an important role in maintaining and regulating homeostasis, are primarily affected. In portal hypertension the organs from which venous outflow is carried out into the portal hepatic vein are primarily affected. Prolonged venous plethora and hypertension in the veins of the portal hepatic vein induce hypoxia, trophic disturbance of these organs, which is a leading factor of their defeat and dysfunction. The development of the latter in the organs can lead to multiorgan failure [3, 8, 9]. It is also known that the structural-functional reorganization of the myocardium may be due to various changes of hemodynamics in the large and small circles of blood circulation and the system of the hepatic portal vein. In the latter, these changes are most often caused by portal hypertension, which often occurs in

cirrhosis and removal of large volumes of liver [7, 9]. Morphometric methods are widely used to study the remodeling of structures and angioarchitectonics of the intraorganic vascular bed of intact organs and in various pathological conditions [1]. It should be noted that the features of remodeling of atrial structures in the conditions of postresection portal hypertension are insufficiently studied.

Objective of the research: to study the features of remodeling of the structures of the atria at postresection portal hypertension histostereometrically.

Materials of the research and their discussion. The peculiarities of remodeling the structures of the atria were histostereometrically studied in 65 adult white male rats, which were divided into 3 groups: the 1- consisted of 20 intact animals, the 2 – 30 rats with postresection portal hypertension, which was modeled by removal of the left and right lateral lobes of the liver [7, 9], the 3- 15 animals with postresection portal hypertension and multiorgan failure. One month after the start of the experiment, rats were euthanized by bloodletting under conditions of thiopental anesthesia. Pieces were cut from the left and right atria, which were fixed in 10% neutral formalin solution and, after passing through alcohols of increasing concentration, placed in paraffin. Microtome sections with a thickness of 5-6 μm after dewaxing were stained with hematoxylin-eosin, van Gizon, Mallory, Weigert, Masson, toluidine blue [2, 6].

Histological micropreparations were used to determine the diameters of cardiomyocytes of the left (DCMLA) and right (DCMRA) atria, diameters of their nuclei (DNCMLA, DNCMRA), nuclear-cytoplasmic relations (NCRCLMA, NCRCLMRA), relative volumes of cardiomyocytes (RVCMLA, RVCMRA), capillaries (RVCLA, RVCRA), stroma (RVSLA, RVSRA), stromal-cardiomyocyte (SCMRLA, SCMRRRA), capillary-cardiomyocyte relations (CCMRLA, CCMRRRA), relative volumes of damaged cardiomyocytes (RVDCMLA, RVDCMRA) [1, 9]. Quantitative indicators were processed statistically. The difference between the comparative morphometric parameters was determined by the criteria of Student and Mann-Whitney [1, 5].

It should be noted that the experimental studies and euthanasia of experimental animals were performed in accordance with the "General Ethical Principles of Animal Experiments" approved by the First National Congress on Bioethics (Kyiv, 2001) and in accordance with the "European Convention for the Protection of Vertebrate Animals other scientific purposes".

Results of the research and their discussion. It was found that resection of the right and left lateral lobes of the liver (58.1 % of its parenchyma) led to the development of

postresection portal hypertension, which was confirmed by dilation and plethora of the portal hepatic vein, splenic and mesenteric veins, venous bed of the small and large intestines, ascites. Fifteen animals were diagnosed with multiorgan failure, manifested by hepatargia, enteral and renal failure.

The obtained histostereometric parameters of the atrial structures obtained as a result of the studies are presented in Table 1. A comprehensive analysis of the quantitative morphological indicators given in the table shows that in the simulated experimental conditions they changed significantly. Thus, the diameter of cardiomyocytes of the left atrium in the conditions of postresection portal hypertension statistically significantly ($p<0.01$) increased by 8.1 % compared with a similar control histostereometric parameter, and in multiorgan failure – by 15.6 %, and the diameters of their nuclei under these experimental conditions increased by 5.6 % and 10.1 %.

Table – Histostereometric characteristics of the atria of the heart of experimental animals
(M±m)

Index	Group of animals		
	1-st	2-nd	3-rd
DCMLA, μm	9.60±0.11	10.38±0.12**	11.10±0.15***
DNCMLA, μm	3.74±0.03	3.95±0.04**	4.12±0.05***
NCRCMLA	0.152±0.003	0.145±0.002*	0.138±0.002**
RVCMLA, %	84.1±1.2	82.2±1.1	80.4±1.1*
RVSLA, %	10.22±0.11	13.10±0.15***	15.50±0.12***
RVCLA, %	5.68±0.07	4.70±0.05***	4.10±0.05***
SCMRLA	0.189±0.003	0.216±0.004**	0.243±0.004***
CCMRLA	0.0675±0.0004	0.0570±0.0006**	0.0509±0.0006**
RVDCMLA, %	2.25±0.03	12.50±0.15***	21.20±0.15***
DCMRA, μm	8.90±0.10	9.45±0.12**	9.76±0.12***
DNCMRA, μm	3.50±0.03	3.63±0.04*	3.68±0.03**
NCRCMRA	0.154±0.003	0.148±0.002	0.142±0.002*
RVCMRA, %	84.1±1.1	82.4±1.2	81.60±1.02
RVSRA, %	10.30±0.15	12.40±0.15***	13.30±0.18***
RVCRA, %	5.70±0.09	5.20±0.06**	5.10±0.04***
SCMRRA	0.190±0.002	0.213±0.003**	0.225±0.003***
CCMRRA	0.0678±0.0005	0.0630±0.0005**	0.0620±0.0005***
RVDCMRA, %	2.20±0.03	7.50±0.06***	14.50±0.12***

Note.* - $p<0.05$; ** - $p<0.01$; *** - $p<0.001$ compared with the 1-st group.

Uneven, disproportionate increases of the studied parameters of cardiomyocytes and their nuclei in the simulated experimental conditions led to violations of the relationship between them, which adequately reflected the nuclear-cytoplasmic relations. The latter in the

2-nd group of observations decreased by 4.6 % ($p < 0.05$), and in the 3-rd (postresection portal hypertension combined with multiorgan failure) – by 9.2 % ($p < 0.01$). Significant changes in nuclear-cytoplasmic relations in the cardiomyocytes of the left atrium in simulated pathological conditions indicated a violation of cellular structural homeostasis [1, 7, 9].

The relative volume of cardiomyocytes in postresection portal hypertension decreased by 1.9 % ($p > 0.05$), and in multiorgan failure – by 3.7 % ($p < 0.05$). In the 2-nd and 3-rd groups of observations, the relative volumes of stroma and microvessels also changed significantly in comparison with the control parameters. Thus, in the 2-nd group the relative volume of the stroma in the left atrium was statistically significantly ($p < 0.001$) increased by 28.2 %, in the 3-rd group – by 51.6 %. The growth of stromal structures in the studied part of the heart was confirmed by stromal-cardiomyocyte relations, which increased by 14.3 % and 28.6 % ($p < 0.001$).

The relative volume of microvessels in the left atrium decreased in studied experiment. Thus, in postresection portal hypertension, it decreased from (5.58 ± 0.07) % to (4.70 ± 0.05) %. There was a statistically significant difference ($p < 0.001$) between the above histostereometric parameters and the last numerical value was lower than the previous one by 15.8 %, with the development of multiorgan failure – by 26.5 % ($p < 0.001$). This was confirmed by capillary-cardiomyocyte relations, which in these groups of observations decreased by 15.5 % and 24.6 % ($p < 0.001$). The relative volume of damaged cardiomyocytes in the left atrium in the 2-nd group of observations increased in 5.5 times, in the 3-rd group – 9.4 times ($p < 0.001$).

Changes of the above histostereometric indicators of the left atrium in postresection portal hypertension and in the occurrence of multiorgan failure indicated a violation of tissue structural homeostasis [1].

Researches have shown that the degree of remodeling of the structures of the right atrium in the studied experimental conditions was less than the left. Thus, the diameter of cardiomyocytes of the right atrium increased by 6.1 % and 9.6 % ($p < 0.001$), and their nuclei – by 3.7 and 5.1 % ($p < 0.01$). Nuclear-cytoplasmic relations in cardiomyocytes of the right atrium in postresection portal hypertension were decreased by 3.8 %, and in the development of multiorgan failure – by 7.8 % ($p < 0.05$).

The relative volume of cardiomyocytes of the right atrium in the 2-nd group of observations was decreased by 1.7 %, in the 3-rd – by 2.5 % ($p > 0.05$), and hemocapillaries, accordingly – by 8.8 % and 10.5 % ($p < 0.001$). The relative volume of the stroma in the studied experimental conditions with a pronounced statistically significant difference

($p < 0.001$) in postresection portal hypertension in the right atrium increased by 20.4 %, and in postresection portal hypertension combined with multiorgan failure by 29.1 %.

The relations between microvessels and cardiomyocytes and between stromal structures and cardiac muscle cells changed significantly in the studied experimental conditions. Thus, stromal-cardiomyocyte relations in the right atrium of the 2-nd group of observations were increased by 12.1 % ($p < 0.01$), in the 3-rd – by 18.4 % ($p < 0.001$) compared with a similar control quantitative morphological indicator. Capillary-cardiomyocyte relations in the right atrium of the 2-nd group of observations with a statistically significant difference ($p < 0.01$) decreased by 7.1 %, in the 3-rd group – by 8.5 % ($p < 0.001$). Significant changes in the relations between stroma and cardiomyocytes, between hemocapillaries and cardiac muscle cells under the studied experimental conditions indicated about pronounced violations of tissue structural homeostasis [1].

It was found that the relative volume of damaged cardiomyocytes of the right atrium in postresection portal hypertension with a high degree of statistically significant difference ($p < 0.001$) increased in 3.3 times, and in combination with postresection portal hypertension with multiorgan failure in 6.6 times.

Histological research of micropreparations of the left and right atria of the 2-nd and 3-rd groups of observations showed pronounced vascular disorders in the form of plethora of mostly venous vessels, perivascular and stromal edema, dystrophic, necrobiotic changes of cardiomyocytes, endothelial cells, stromal structures, foci of infiltration and sclerosis. The detected morphological changes dominated in the left atrium in postresection portal hypertension combined with multiorgan failure and correlated with histostereometric parameters.

Significant histopathological and histostereometric changes in the left atrium indicate that this part of the myocardium in postresection portal hypertension is the most functionally overloaded and more altered compared to the right atrium. Simulated hemodynamic changes, their severity, the degree of violations of tissue and cellular structural homeostasis, as evidenced by the identified morphological changes and histostereometric parameters can lead to dysfunction of the studied organs.

Conclusions. Postresection portal hypertension leads to pronounced remodeling of the structures of the left and right atria, characterized by hypertrophy of cardiomyocytes, changes in their nuclear-cytoplasmic relations, an increase of the relative volumes of stroma, damaged cardiac muscle cells, pronounced disorders of tissue and cellular structural homeostasis. The

revealed morphological changes dominated in the left atrium at a combination of postresection portal hypertension with multiorgan failure.

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